Case Report
JCAM

A case of weill-marchesani syndrome with a novel mutation and vitamin d deficiency

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Abstract

Weill-Marchesani syndrome is an inherited connective tissue disorder. It is characterized by various ocular abnormalities and some skeletal problems. It is rarely seen in the world, but the clinical complications are significant and may require some interventions such as eye surgery, physical therapy or orthopedic procedures. Here we report on an eleven year old female with glaucoma, ectopia lentis, microspherophakia, brachydactyly and vitamin D deficiency from Sivas, Turkey. She was suffering from Weill-Marchesani syndrome with ADAMTS10 mutation.

Keywords

Weill-Marchesani Syndrome, Microspherophakia, Glaucoma, Brachydactyly, Vitamin D Deficiency

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Introduction

Weill-Marchesani syndrome (WMS) is an inherited disorder of connective tissue associated with abnormalities of the lens, proportionate short stature, brachydactyly, joint stiffness and sometimes, heart defects. It was first described by Georges Weill in 1932 and analyzed in more detail by Oswald Marchesani in 1939 [1]. This syndrome is caused by the mutations of ADAMTS10*, LTPBP2, ADAMTS17* and FBN1 genes [2]. The ocular problems may include microspherophakia, myopia, lens luxation, corneal changes and glaucoma which may lead to blindness [3]. In this report, we present a case of WMS with angle-closure glaucoma and vitamin D deficiency as an unusual feature for WMS.

Case Report

An eleven year old female who had short stature, joint stiffness, brachydactyly and visual problems was referred to Cumhuriyet University, Research Hospital (Figure 1, 2). Her height was 115 cm and her weight was 26 kg. She was examined at the ophthalmology polyclinic. Our patient had alternating exotropia of about 30D. The initial best-corrected visual acuity was 0.2 (-11.00 Dsph (-1.75 Dcyl A ~160) in the right eye (RE) and 0.3 (-10.00 Dsph (-0.75 Dcyl A ~110) in the left eye (LE). Intraocular pressure (IOP) measured by Goldmann Applanation Tonometry was 55 mmHg in the right eye and 37 mmHg in the left one. The central corneal thickness was 707/668 µm.

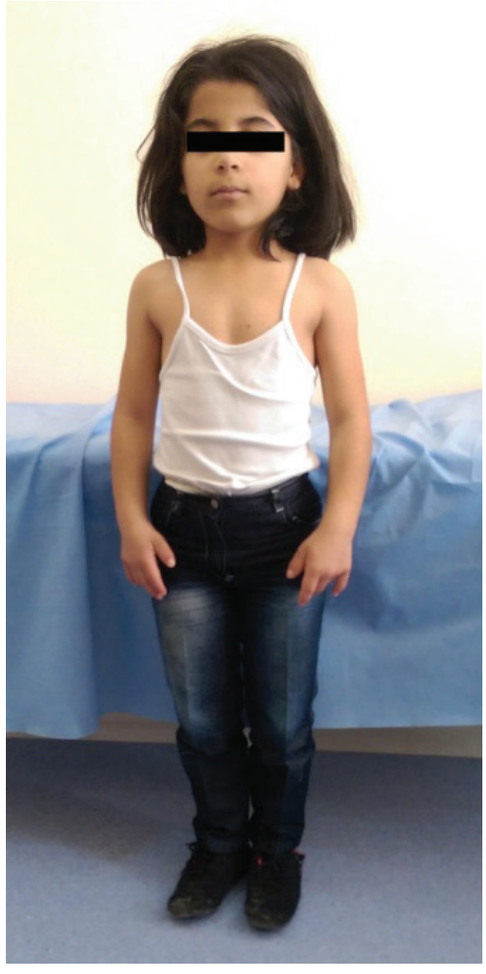

Figure 1. Short stature of the patient.

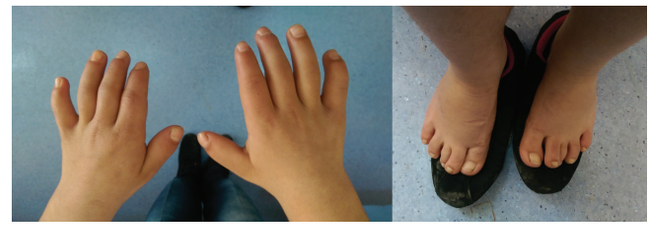

Figure 2. Brachydactyly of the hands and feet.

Slit lamp examination revealed bilateral clear corneas, shallow anterior chambers (the anterior chamber of the right eye was extremely narrow and the iris bulged forward), marked iridodonesis and phacodonesis. After pupillary dilatation, the entire lens equator was visible within the pupil; there was an increased curvature of the anterior aspect of the lenses, suggestive of microspherophakia (Figure 3). The zonules were stretched, but unbroken.

Figure 3. Microspherophakic lenses in the right and left eye.

The optic disc was pale and the cup-to-disc (C/D) ratio was 0.9 in the right eye and 0.7 in the left eye. Indentation gonioscopy showed bilateral closed angles. Antiglaucoma medications were administered to the eyes with increased IOP and angle-closure glaucoma (three topical medications, eye drops, latanoprost 0.005%, timolol 0.5% and brimonidine 0.2%). Because of the formation of pupillary block caused by forward movement of the lens, peripheral iridotomy was added to treatment. YAG laser peripheral iridotomy was done by choosing a thin portion of the peripheral iris under maximum illumination at the slit lamp. After the intervention, the patient's best-corrected visual acuity was 0.5 (-15.00 Dsph) in the right eye and 0.6 (-12.00 Dsph) in the left eye. IOP measured by Goldmann Applanation Tonometry was 18 mmHg in the right eye and 19 mmHg in the left eye without any antiglaucoma medications. The next slit lamp examination also revealed bilateral transparent corneas, near normal anterior chamber depth, and effective peripheral iridotomy. The optic disc was pale and the cup-to-disc (C/D) ratio was 0.7 in both eyes. We detected homozygous mutation in *ADAMTS10* gene (c.1708delT) in exon 14 by sequencing with Mutation Surveyor DNA Variant and Sequence Analysis Software Version: 5.0 (SoftGenetics, USA). The patient also suffered from vitamin D deficiency (5ng/ml). DXA scanning of the patient showed normal bone mineral density (BMD). She had grade 1 pulmonary valve regurgitation and mild mitral and tricuspid regurgitation. She had no intellectual disability. This patient was diagnosed with Weill-Marchesani syndrome on the basis of molecular analysis and clinical signs such as optic disorders, short stature and brachydactyly. All examinations and researchs were performed on the patient after informed consent was received from the family.

Discussion

Weill-Marchesani syndrome is a rare systemic connective tissue disorder. Most cases of WMS have been described by ophthalmologists, because ocular symptoms (microspherophakia, high myopia and secondary glaucoma) are at the forefront in this syndrome [4]. An abnormal increase in lens curvature leads to enhanced refractive power. The increased lens thickness results in a narrow anterior chamber and angles. The lens moves forward due to zonular relaxation, which leads to pupillary block and elevated IOP. Peripheral iridotomy is beneficial in pupillary block. Additionally, removal of the microspherophakia can provide the control of intraocular pressure and it helps to preserve vision. Advanced glaucoma in WMS should be treated with combined glaucoma surgery with lens extraction. The patient in this case report had early glaucoma and she benefited from the peripheral iridotomy. After 7 months of follow-up, the patient had well-controlled intraocular pressure, transparent cornea, and near normal anterior chamber depth. The requirement of surgery depends on the course of glaucoma.

ADAMTS10 gene mutations are responsible for many cases with this syndrome. This gene is located in the short arm of chromosome 19 (19p13) and ADAMTS is a glycoprotein family that has been shown to be involved in various biological processes such as connective tissue organization, coagulation, inflammation, angiogenesis, and cell migration [5]. ADAMTS10 has several N-linked glycosylation sites in different protein domains. Extracellular secretion of ADAMTS10 is important for its function in the extracellular matrix. The function of the mutated ADAMTS10 is disrupted and this mutation causes the WMS phenotype [6].

We present a case of WMS with vitamin D deficiency and mild cardiac defects (Grade 1 pulmonary valve regurgitation and mild mitral and tricuspid regurgitation). Our patient had main systemic and ocular features of WMS. She was suffering from short stature, brachydactyly, stiff joints, glaucoma, ectopia lentis and microspherophakia. Ectopia lentis may be associated with the microspherophakia of the lens. Microspherophakia and forward movement of the lens might induce pupillary block. Most of the patients with WMS had angle closure glaucoma. When Weill-Marchesani syndrome is caused by mutations in ADAMTS10 or *LTPBP2* gene, it has an autosomal recessive pattern of inheritance. On the other hand, WMS caused by FBN1 mutation is inherited in an autosomal dominant manner.

There may be some significant differences between autosomal recessive and dominant cases for the clinical findings including microspherophakia, ectopia lentis, joint limitations and cardiac defects [7]. For example, heart defects are usually observed in the recessive form [8].

There was a homozygous mutation of ADAMTS10 gene in our patient and her disease was an autosomal recessive WMS. It was caused by a novel mutation (c.1708delT). Her parents were healthy individuals and they were heterozygous for this mutation. This was a consanguineous marriage. Vitamin D deficiency was an interesting sign that accompanied the disease. Our case had severe vitamin D deficiency (5ng/ml) and vitamin D treatment was started but BMD of the patient was close to normal with DXA screening. We did not find osteoporosis status in our patient. A possible relationship between WMS and metabolism of vitamin D is not known. It requires more researchs and data. On the other hand, the cause of vitamin D deficiency in our patient may be the deprivation of sunlight.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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